

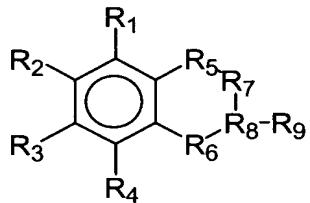
In the Claims

Claims 1-6 (Cancelled)

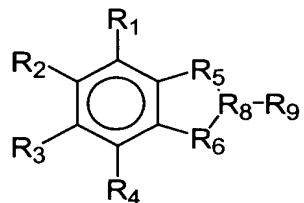
7. (Currently Amended) An angiogenesis inhibitory composition comprising an angiogenesis inhibiting compound and an anti-inflammatory drug, wherein the angiogenesis inhibiting compound is selected from:

(1) a compound ~~selected from~~ of the formula

A)

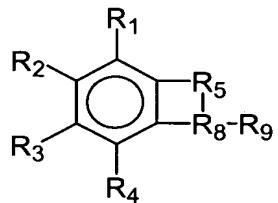


B)



or

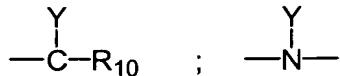
C)



wherein

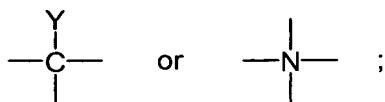
R₁-R₄ are each independently ~~selected from~~ -H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic

and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, $-XO_n$ or $-O-XO_n$, where $X=N$ and $n=2$, $X=S$ and $n=2$ or 3, or $X=P$ and $n=1-3$; and halogens; R_5-R_7 are each independently selected from



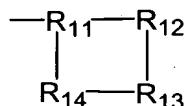
E
CM

or $-O-$, where Y is absent and R_{10} is $=O$, or Y and R_{10} are each independently the same as R_4 ; $=O$; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, $-XO_n$ or $-O-XO_n$, where $X=N$ and $n=2$, $X=S$ and $n=2$ or 3, or $X=P$ and $n=1-3$; and halogens; where R_8 is independently selected from:

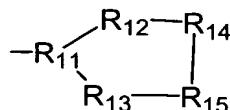


and R_9 is a moiety selected from

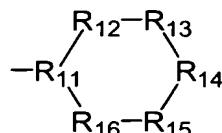
D)



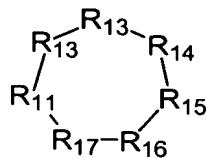
E)



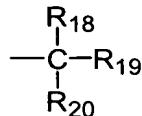
F)



G)



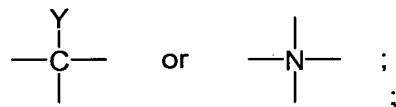
or H)



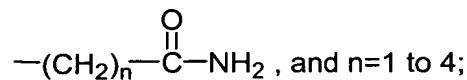
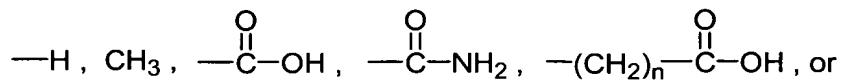
wherein each of R₁₂-R₁₇ is independently the same as R₅



wherein R₁₁ is independently the same as R₈

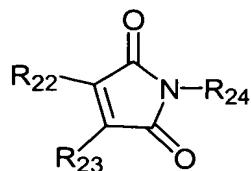


and wherein R₁₈, R₁₉ and R₂₀ are each independently selected from



with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound selected from of the formula

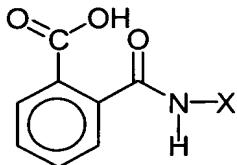


where R₂₂ and R₂₃ are each independently H, F, Cl, Br, I, CH₃, or -CH₂-CH₃; and R₂₄ is H,

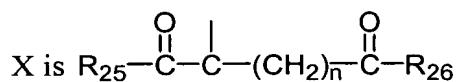
CH₃, or -CH₂-CH₃;

and

(3) a compound ~~selected from~~ of the formula



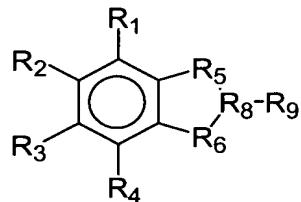
where X is R₆ as defined in (1) above, or



and R₂₅ and R₂₆ are independently -OH, -H, or -NH₂, and n = 1 through 4.

8. (Currently Amended) The angiogenesis inhibitory composition of Claim 7 wherein the angiogenesis inhibiting compound ~~has~~ is of the formula

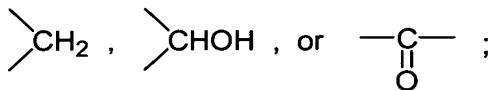
B)



wherein R₁-R₄ are defined in Claim 7 and R₅ and R₆ are independently ~~selected from~~



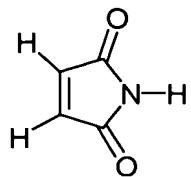
and R₉ is ~~selected from~~ F) or H) wherein R₁₄ and R₁₆ are each independently ~~selected from~~



and R₁₅ is -O- or $\begin{array}{c} R_{21} \\ | \\ -N- \end{array}$, where R₂₁ is H, CH₃, or OH.

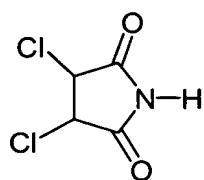
9. (Currently Amended) The angiogenesis inhibitory composition of claim 7 wherein the angiogenesis inhibiting compound is ~~selected from~~

I)

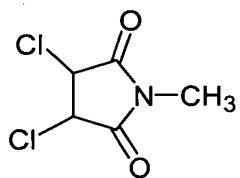


J)

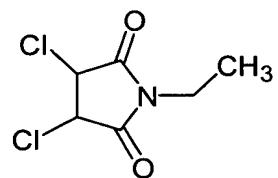
Et
Et
Am



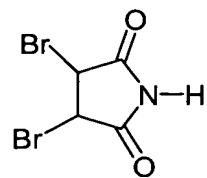
K)



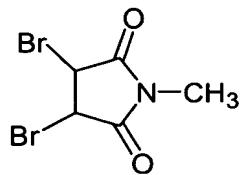
L)



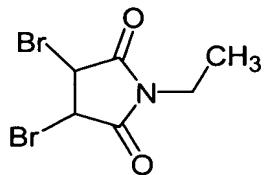
M)



N)

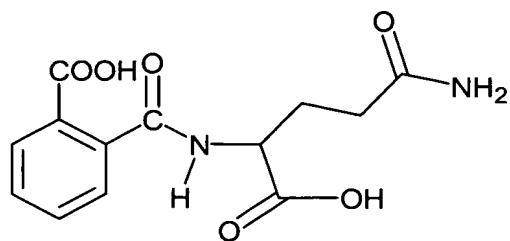


O)

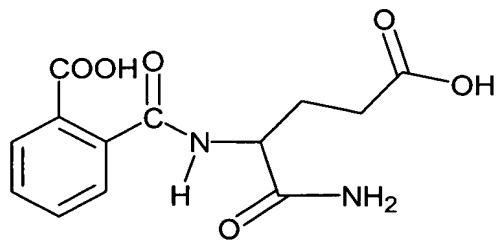


*C
C
C*

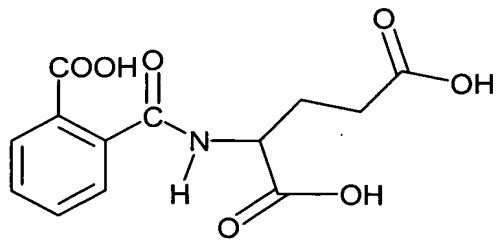
P)



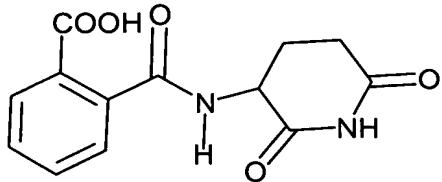
Q)



R)



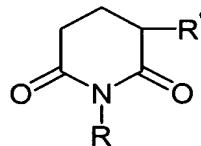
or S)



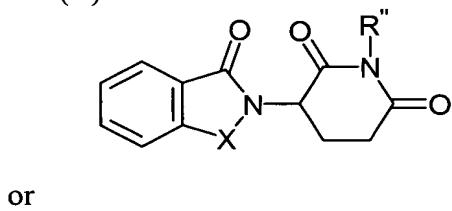
10. (Currently Amended) The angiogenesis inhibitory composition of
 Claim 7 wherein the angiogenesis inhibiting compound is ~~a selected from~~ metabolites of
 thalidomide, thalidomide analogs, epoxides of thalidomide, hydrolysis products thereof,
 hydrolysis products of thalidomide, EM-12, metabolites of EM-12, epoxides of EM-12,
 hydrolysis products thereof, EM-138, metabolites of EM-138, epoxides of EM-138,
 hydrolysis products thereof, N-phthaloyl-DL-glutamic acid (PGA), N-phthaloyl-DL-glutamine
 anhydride, or mixture thereof.

11. (Currently Amended) The angiogenesis inhibitory composition of
 Claim 10 wherein the angiogenesis inhibiting compound is ~~selected from~~

(I)



(II)



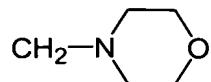
or

wherein

R is ~~selected from~~ H, (C₁-C₆)alkyl, phenyl, or benzyl; and R' is ~~selected from~~
 phthalimido or succinimido;

wherein

X is CH₂ or C=O; and R'' is H, -CH₂CH₃, -C₆H₅, -CH₂C₆H₅, -CH₂CH=CH₂, or



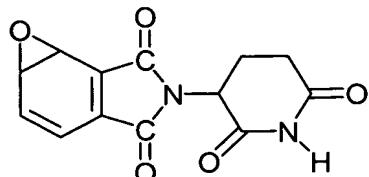
or (III) hydrolysis products of (II)

wherein

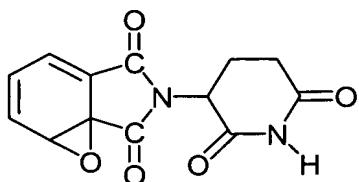
R" is H and the piperidino ring or both the piperidino and the imido ring are hydrolyzed.

12. (Currently Amended) The angiogenesis inhibitory composition of
Claim 10 wherein the angiogenesis inhibiting compound is ~~selected from~~

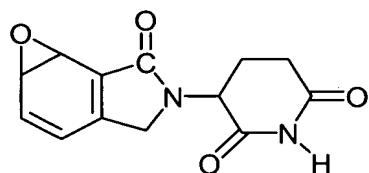
III)



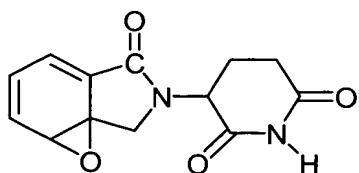
IV)



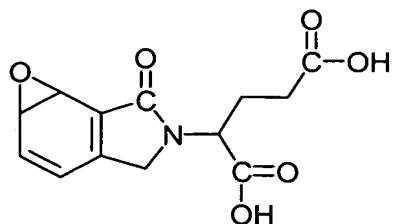
V)



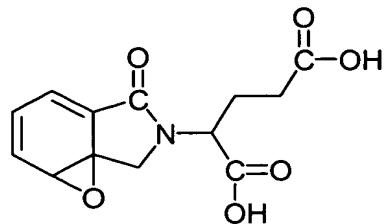
VI)



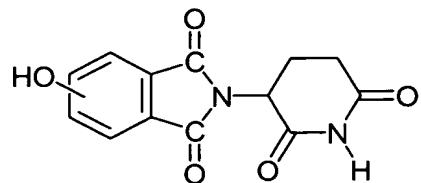
VII)



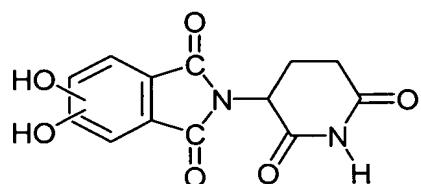
VIII)



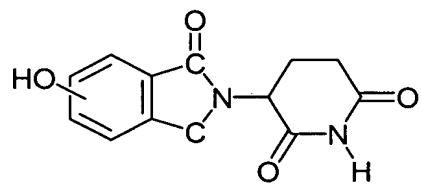
IX)



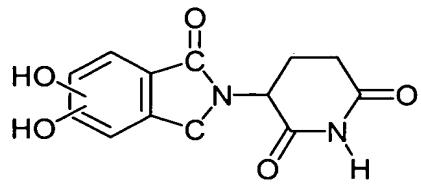
X)



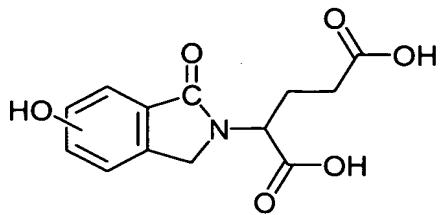
XI)



XII)

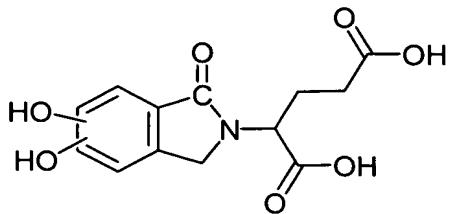


XIII)



or XIV)

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cmf*



Claims 13-14 (Cancelled)

15. (Currently Amended) A method for inhibiting angiogenesis in a human or animal comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an antiinflammatory compound, with the proviso that the angiogenesis inhibiting compound is not thalidomide.

Claims 16-18 (Cancelled)

19. (Currently Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal in need of such treatment a composition comprising an angiogenesis inhibiting compound and an antiinflammatory compound, with the proviso that the angiogenesis inhibiting compound is not thalidomide.

20. (Currently Amended) The method of Claim 19 wherein the angiogenesis dependent disease is selected from macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phylectenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal

ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, veinocclusion, artery occlusion, cartoid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosis, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

21. (Previously Added) The angiogenesis inhibitory composition of Claim 7 wherein the antiinflammatory drug is a steroid.

22. (Currently Amended) The angiogenesis inhibitory composition of Claim 21 wherein the steroid is ~~selected from~~ cortisol, corticosterone, hydrocortisone, hydrocortisol, cortisone, prednisone, prednisolone, dexamethasone, beclomethasone, betamethasone, mometasone, mometasone furoate, budesonide, triamcinolone acetonide, or fluticasone.

23. (Currently Amended) An angiogenesis inhibitory composition of Claim 7 wherein the anti-inflammatory drug is a nonsteroidal, anti-inflammatory drug (NSAID).

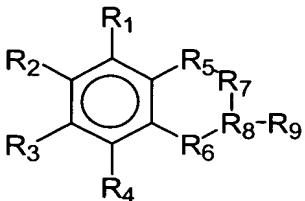
24. (Currently Amended) The angiogenesis inhibitory composition of Claim 23 wherein the nonsteroidal, anti-inflammatory drug NSAID is ~~selected from~~ aspirin, acetominophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguaiaretic acid (NDGA), sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398 (~~a cyclooxygenase-2 inhibitor~~), cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecasa, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, flotafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, pirprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, or tenoxicam.

25. (Currently Amended) The angiogenesis inhibitory composition of
Claim 23 wherein the nonsteroidal, anti-inflammatory drug NSAID is selected from
indomethacin or sulindac.

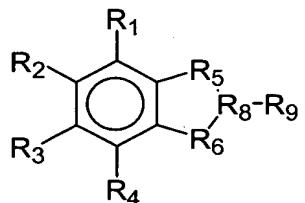
26. (Currently Amended) A method for inhibiting angiogenesis in a
human or animal comprising administering to the a human or animal in need of such
inhibition a composition comprising an angiogenesis inhibiting compound and an anti-
inflammatory compound, wherein the angiogenesis inhibiting compound is selected from:

(1) a compound selected from the formula

A)

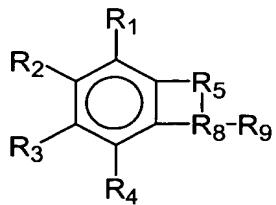


B)



or

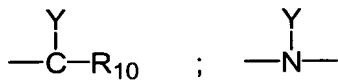
C)



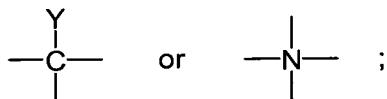
wherein

R₁-R₄ are each independently selected from -H; -OH; =O; straight or branched chain
alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic
and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester,

or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, $-XO_n$ or $-O-XO_n$, where $X=N$ and $n=2$, $X=S$ and $n=2$ or 3 , or $X=P$ and $n=1-3$; and halogens; R_5-R_7 are each independently selected from

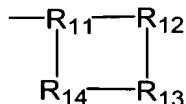


or $-O-$, where Y is absent and R_{10} is $=O$ or Y and R_{10} are each independently the same as R_8 ; $-H$; $-OH$; $=O$; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, $-XO_n$ or $-O-XO_n$, where $X=N$ and $n=2$, $X=S$ and $n=2$ or 3 , or $X=P$ and $n=1-3$; and halogens; where R_8 is independently selected from:

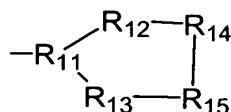


and R_9 is a moiety selected from

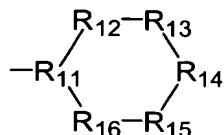
D)



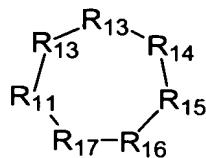
E)



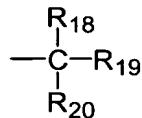
F)



G)

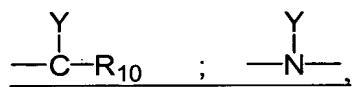


or H)

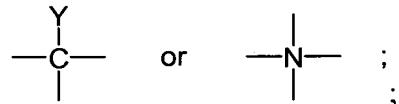


wherein each of R_{12} - R_{17} is independently the same as R_5

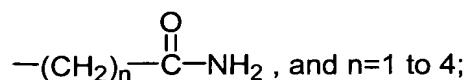
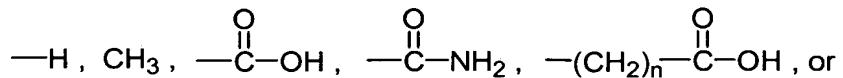
E
X
C
M



wherein R_{11} is independently the same as R_8

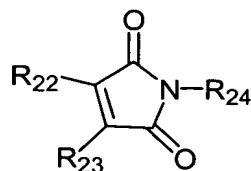


and wherein R_{18} , R_{19} and R_{20} are each independently selected from



with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound selected from of the formula



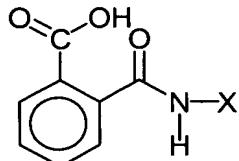
where R_{22} and R_{23} are each independently H, F, Cl, Br, I, CH_3 , or

-CH₂-CH₃;

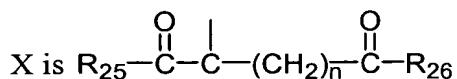
and R₂₄ is H, CH₃, or -CH₂-CH₃;

and

(3) a compound ~~selected from~~ of the formula



E
C
u
t where X is R₆ as defined in (1) above, or



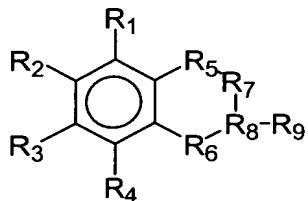
and R₂₅ and R₂₆ are independently -OH, -H, or -NH₂, and n = 1 through 4.

27. (Currently Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal in need of such treatment a composition comprising an angiogenesis inhibiting compound and an antiinflammatory compound

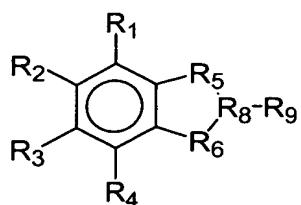
wherein the angiogenesis inhibiting compound is ~~selected from~~:

(1) a compound ~~selected from~~ of the formula

A)

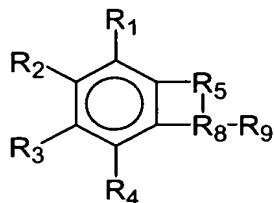


B)



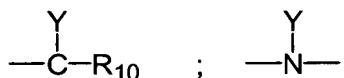
or

C)

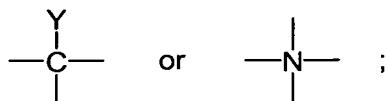


wherein

*R*₁-*R*₄ are each independently selected from -H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, -XO_n or -O-XO_n, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens; R₅-R₇ are each independently selected from

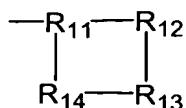


or -O-, where Y is absent and R₁₀ is =O, or Y and R₁₀ are each independently the same as R₁-H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino, -XO_n or -O-XO_n, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens; where R₈ is independently selected from:

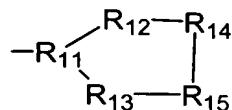


and R₉ is a moiety selected from

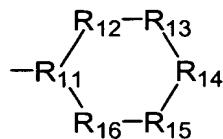
D)



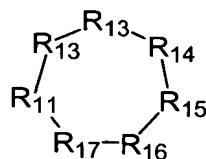
E)



F)

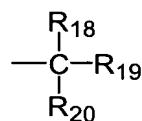


G)

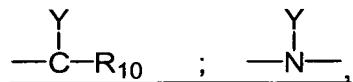


*Et
Or*

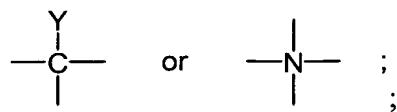
H)



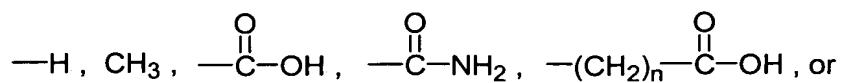
wherein each of R_{12} - R_{17} is independently the same as R_5

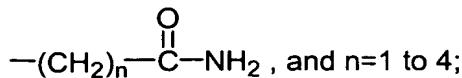


wherein R_{11} is independently the same as R_8



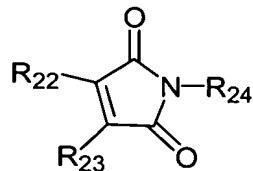
and wherein R_{18} , R_{19} and R_{20} are each independently selected from





with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound selected from the formula



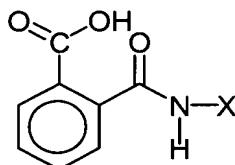
where R_{22} and R_{23} are each independently H, F, Cl, Br, I, CH_3 , or

$-\text{CH}_2-\text{CH}_3$;

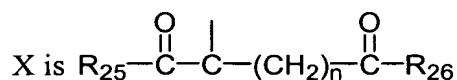
and R_{24} is H, CH_3 , or $-\text{CH}_2-\text{CH}_3$;

E
X
and
Ch

(3) a compound selected from of the formula



where X is R_6 as defined in (1) above, or



and R_{25} and R_{26} are independently $-\text{OH}$, $-\text{H}$, or $-\text{NH}_2$, and $n = 1$ through 4.

28. (Currently Amended) The method of Claim 27 wherein the angiogenesis dependent disease is selected from macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasias, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Chron's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior

limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phylectenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Page's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosis, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

29. (Currently Amended) The angiogenesis inhibitory composition of Claim 7 wherein ~~the dosage of~~ the angiogenesis inhibiting compound is in a dosage of between about 0.1 to about 300 mg/kg/day.

30. (Currently Amended) The angiogenesis inhibitory composition of Claim 7-29 wherein the dosage of the angiogenesis inhibiting compound is between about 0.5 to about 50 mg/kg/day.

31. (Currently Amended) The angiogenesis inhibitory composition of Claim 7-30 wherein the dosage of the angiogenesis inhibiting compound is between about 1 to about 10 mg/kg/day.

32. (Previously Added) The method of Claim 26 wherein the composition comprises a formulation suitable for oral, rectal, ophthalmic, nasal, topical, vaginal, or parenteral administration.

33. (Previously Added) The method of Claim 22 wherein the composition comprises a formulation suitable for oral, rectal, ophthalmic, nasal, topical, vaginal, or parenteral administration.

34. (Currently Amended) The method of Claim 26 wherein ~~the dosage of~~ the angiogenesis inhibiting compound is in a dosage of between about 0.1 mg/kg/day to about 300 mg/kg/day.

35. (Currently Amended) The method of Claim 26 34 wherein the dosage of the angiogenesis inhibiting compound is between about 0.5 mg/kg/day to about 50 mg/kg/day.

36. (Currently Amended) The method of Claim 26 35 wherein the dosage of the angiogenesis inhibiting compound is between about 1 mg/kg/day to about 10 mg/kg/day.

37. (Previously Added) The method of Claim 27 wherein the dosage of the angiogenesis inhibiting compound is between about 0.1 mg/kg/day to about 300 mg/kg/day.

38. (Currently Amended) The method of Claim 27 37 wherein the dosage of the angiogenesis inhibiting compound is between about 0.5 mg/kg/day to about 50 mg/kg/day.

39. (Currently Amended) The method of Claim 27 38 wherein the dosage of the angiogenesis inhibiting compound is between about 1 mg/kg/day to about 10 mg/kg/day.

Claims 40-42 (Cancelled)

43. (Currently Amended) An angiogenesis inhibitory composition of Claim 11 wherein the anti-inflammatory drug is a nonsteroidal, anti-inflammatory drug (NSAID).

44. (Currently Amended) The angiogenesis inhibitory composition of Claim 43 wherein the nonsteroidal, anti-inflammatory drug NSAID is selected from aspirin, acetominophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguaiaretic acid (NDGA), sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398 (a cyclooxygenase-2 inhibitor), cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecasa, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, flocafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, pirprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, or tenoxicam.

45. (Currently Amended) The method of Claim 15, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (NSAID).

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cont

46. (Currently Amended) The method of Claim 19, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (~~NSAID~~).

47. (Currently Amended) The method of Claim 26, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (~~NSAID~~).

48. (Currently Amended) The method of Claim 27, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (~~NSAID~~).